

Table S3 Comparison of valproic acid (VPA) and 4-ene-VPA maximal concentrations (C_{max}) predicted by ontogeny-based PBPK approach *versus* conventional allometric scaling methods under various dosage for distinct pediatric age groups

Approach	C_{max} (mg/L)	Neonate		Infant		Toddler and preschooler		School age		Adolescent	
		VPA	4-ene-VPA	VPA	4-ene-VPA	VPA	4-ene-VPA	VPA	4-ene-VPA	VPA	4-ene-VPA
The study (ontogeny-based PBPK approach)											
	31.25 mg/BID	66.92	0.10	31.19	0.05	20.14	0.03	12.21	0.02	6.89	0.01
	62.50 mg/BID	136.45	0.19	61.46	0.10	37.39	0.07	23.04	0.04	13.31	0.03
	125.00 mg/BID	277.71	0.39	124.85	0.20	75.24	0.13	43.21	0.09	25.01	0.06
	250.00 mg/BID	568.81	0.81	252.78	0.41	152.29	0.26	87.7	0.18	47.33	0.11
	375.00 mg/BID	867.97	1.23	382.45	0.62	229.69	0.40	132.38	0.27	71.69	0.17
	437.50 mg/BID	1019.79	1.45	447.87	0.72	268.58	0.46	154.77	0.31	83.99	0.20
	468.75 mg/BID	1096.18	1.56	480.71	0.78	288.08	0.50	165.98	0.33	90.14	0.21
	500.00 mg/BID	1172.85	1.67	513.63	0.83	307.61	0.53	177.19	0.36	96.25	0.23
Allometric scaling methods											
	Fried's or Young's rule	7.54	0.01	36.51	0.06	80.98	0.14	64.48	0.14	49.45	0.11
	Clark's rule	58.46	0.09	62.62	0.10	72.67	0.13	78.05	0.17	75.82	0.16
	BSA-based	141.74	0.22	119.48	0.20	118.59	0.21	98.56	0.21	82.37	0.17

The usual dose of valproic acid for adult is 500 mg BID.